Claims

1 A method for preparing particles of an active substance having a layer of an additive at the particle surfaces, the method involving dissolving both the active substance and the additive in a vehicle to form a target solution, and contacting the target solution with an anti-solvent fluid to simultaneously disperse and extract the vehicle from the target solution, to cause the active substance and additive to coprecipitate.

2 A method according to claim 1, wherein the additive is a taste and/or odour masking agent.

3 A method according to claim 1, wherein the active substance comprises a pharmaceutically active substance.

4 A method according to claim 1, wherein the active substance is dissolved in a first fluid and the additive in a second fluid, and the first and second fluids are mixed, so as to form the target solution, at or immediately before the target solution contacts the anti-solvent fluid and precipitation occurs.

5 A method according to claim 1, wherein the anti-solvent fluid is a supercritical fluid.

6 A method according to claim 1, wherein the precipitation rate of the active substance is higher than that of the additive under the operating conditions used.

7 A method according to claim 4, wherein the two vehicle fluids have significantly different solubilities in the anti-solvent fluid under the operating conditions used.

8 A method according to claim 7, wherein the solubility of the active substance in the first vehicle fluid is significantly lower than the solubility of the additive in the second vehicle fluid.

9 A method according to claim 1, wherein, under the operating conditions used, the active substance precipitates in a crystalline form and the additive in an amorphous form.

10 A method according to claim 1, wherein, under the operating conditions used, the active substance precipitates in a crystalline form which is significantly longer in one dimension than in at least one other dimension, and/or its crystals grow significantly faster in one dimension than in at least one other dimension.

11 A method according to claim 4, wherein the additive has a significantly higher solubility in the anti-solvent fluid, under the operating conditions used, than does the active substance.

12 A method according to claim 1, wherein the active substance and the additive have a low compatibility with one another.

13 A method according to claim 12, wherein the active substance and the additive have a solubility in one another of less than 30 % w/w.

14 A method according to claim 1, wherein on assigning a value of 1, 2 or 3 to each of the active substance and the additive, 1 meaning that the material in question has a low polarity, 3 meaning that it is highly polar and 2 meaning that it is of intermediate polarity, the active substance and the additive have different polarity values.

15 A method according to claim 1, which is carried out at a temperature and pressure such that the anti-solvent fluid is in a supercritical form but is more liquid-like than gas-like in its properties.

16 A method according to claim 1, which is carried out at a temperature between 1 and 1.1 times the critical temperature T_c (in Kelvin) of the anti-solvent fluid, and/or at a pressure between 1 and 1.5 times the critical pressure P_c of the anti-solvent fluid.

17 A method according to claim 16, which is carried out at a temperature between 298 and 323 K, and a pressure between 70 and 120 bar.

18 A method according to claim 1, wherein the vehicle and the anti-solvent fluid have less than complete miscibility with one another.

19 A method according to claim 1, wherein the active substance is a crystalline material and the relative concentrations of the active substance and the additive in the target solution are such that:

(a) the active substance is able to precipitate in a crystalline form under the operating conditions used; whilst at the same time:

(b) there is sufficient additive to generate an additive-rich, preferably active-free or substantially so, layer at the particle surfaces.

20 A particulate coformulation of an active substance and an additive, which is a solid dispersion of one component in the other, but which has a finite gradient in the relative additive concentration, which concentration increases radially outwards from the core to the surface of the particles.

21 A particulate coformulation according to claim 20, the particles of which have an additive-rich surface region but do not possess separate core and coating layers with a distinct physical boundary between them.

22 A particulate coformulation according to claim 20, wherein the rate of change in additive concentration, across the particle radius, is continuous rather than stepped.

23 A particulate coformulation according to any claim 20, wherein the active substance:additive ratio, at the particle surfaces, is sufficiently low for the additive to form, effectively, a protective surface layer around the active substance.

24 A particulate coformulation according to claim 20, wherein the additive is a taste and/or odour masking agent, and wherein the active substance:additive weight ratio, at the particle surfaces, is sufficiently low for there to be no detectable release of the active substance for at least 30 seconds after the coformulation comes into contact with saliva in a consumer's mouth.

25 A particulate coformulation according to claim 20, wherein the particle surfaces contain, at their outer limits, no exposed active substance.

26 A particulate coformulation according to claim 20, which is or comprises a pharmaceutical or nutriceutical agent or a foodstuff.

27 A particulate coformulation according to claim 20, wherein the additive is an oligomeric or polymeric material.

28 A particulate coformulation according to claim 20, wherein the additive is a substance capable of protecting the active substance from external effects such as heat, light, moisture, oxygen or chemical contaminants, and/or of reducing incompatibilities between the active substance and another material with which it needs to be processed or stored, and/or of delaying, slowing or targetting the release of the active substance, and/or of masking the flavour and/or odour of the active substance, when applied to the surface of the active substance.

29 A particulate coformulation according to claim 28, wherein the additive is a taste and/or odour masking agent.

30 A particulate coformulation according to claim 20, wherein the active substance comprises a pharmaceutically active substance.

31 A particulate coformulation according to claim 30, wherein both the active substance and the additive comprise pharmaceutically active substances for co-administration.

32 A particulate coformulation according to claim 20, wherein the active substance is a carrier, diluent or bulking agent for the additive.

33 A particulate coformulation according to claim 20, wherein the active substance is present in a crystalline form and the additive is present in an amorphous form.

34 A particulate coformulation according to claim 33, wherein differential scanning calorimetry (DSC) and/or X-ray diffraction (XRD) analysis of the coformulation indicates reduced active substance crystallinity compared to that of the active substance alone.

35 A particulate coformulation according to claim 34, wherein the active substance:additive concentration ratio is such that the active substance demonstrates between 20 and 95 % crystallinity as compared to the active substance starting material.

36 A particulate coformulation according to claim 20, which is in the form of either spherical or approximately spherical particles having a volume mean diameter of between 0.5 and 100 μm, or of needle-like particles having a volume mean length between 5 and 100 μm and a volume mean thickness between 0.5 and 5 μm, or of plate-like particles having a volume mean thickness between 0.5 and 5 μm.

37 A particulate coformulation according to claim 20, wherein the active substance concentration is 70 % w/w or greater.

38 A particulate coformulation according claim 37, wherein the active substance concentration is 80 % w/w or greater.

39 A particulate coformulation according to claim 20, wherein the additive concentration is 10 % w/w or greater.

40 A particulate coformulation of an active substance and an additive, which is obtainable by a method according to any one of claims 1 to 19.

41 A pharmaceutical composition which includes a coformulation according to any one of claims 20 to 39.

42 A foodstuff or nutriceutical composition which includes a coformulation according to any one of claims 20 to 39.